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3	2	luteolin same (blood near2 glucose)	USPAT; EPO; JPO; DERWENT	2002/09/04 14:10
4	1	luteolin same hyperglycemia	USPAT; EPO; JPO; DERWENT	2002/09/04 14:10

Quercetin

October 31, 1995

Effect of flavonoids on arachidonic acid metabolism

Flavonoids, particularly quercetin, are inhibitors of allergic (IgE-mediated) mediator release from mast cells and basophils (Fewtrell and Gomperts, 1977 and Middleton and Drzewiecki, 1984). In previous studies reported from our laboratories (Hope et al., 1983) quercetin inhibited not only IgE-mediated allergic mediator release from mast cells but also IgG-mediated histamine and SRS-A (peptidoleukotriene) release from chopped lung fragments from actively sensitized guinea pigs. Interestingly, quercetin was much more potent as an inhibitor of the release of SRS-A than histamine, suggesting that it might also inhibit the biosynthesis of SRS-A. Subsequently we demonstrated that quercetin was an effective inhibitor of Æ5-lipoxygenase. This property of the compound most likely accounts for its effect on peptidoleukotriene biosynthesis. The studies reported herein further expand on these observations by evaluating the activities of a variety of standard flavonoids on Æ5-lipoxygenase and other enzymes known to be involved in the metabolism of arachidonic acid in cells. Compounds such as the flavonoid, quercetin, which exhibit both allergic mediator release activity and selective inhibition of the biosynthesis of proinflammatory arachidonic acid metabolites may be interesting prototypes which will lead to the discovery of very effective antiallergic and antiinflammatory agents.*Welton AF, Tobias LD, Fiedler-Nagy C, et al. Effect of flavonoids on arachidonic acid metabolism. Prog Clin Biol Res 213:231-242; 1986.*

Anti-inflammatory activity of benzopyrones that are inhibitors of cyclo- and lipo-oxygenase

The anti-inflammatory activity of three benzo-pyrones with prevalent lipo-oxigenase-inhibitory activity was studied using the Croton oil ear test in mice, in comparison with nordihydroguaieretic acid (NDGA) and indomethacin. Kaempferol, quercetin and NDGA possess a strong and prolonged anti-inflammatory effect, whereas the action of indomethacin appears relevant, but not long-lasting. In contrast the anti-inflammatory activity of esculetin is rather weak, but persistent.*Della Loggia R, Ragazzi E, Tubaro A, et al. Anti-inflammatory activity of benzopyrones that are inhibitors of cyclo- and lipo-oxygenase. Pharmacol Res Commun 20:S91-S94; 1988.*

Antiulcer and gastroprotective effects of quercetin: a gross and histologic study

This study was designed to determine the cytoprotective properties of quercetin and the involvement of endogenous prostaglandins in mucosal injury produced by absolute ethanol. Gastric glands were also analyzed histologically. Oral pretreatment with the highest dose of quercetin (200 mg/kg), 120 min before absolute ethanol, was most effective in necrosis prevention. Subcutaneous administration of indomethacin (10 mg/kg) to the animals treated with quercetin (200 mg/kg) partially inhibited gastric protection. All treated groups showed a marked increase in the amount of gastric mucus although this increase was less in animals pretreated with indomethacin. Total proteins and the hexosamine content decreased in the groups receiving indomethacin. The histomorphometric evaluation of the gastric damage confirmed a significant increase in mucus production accompanied by a parallel reduction of gastric lesions with the highest dose of quercetin tested.*Alarcon de la Lastra C, Martin MJ, Motilva V. Antiulcer and gastroprotective effects of quercetin: a gross and histologic study. Pharmacology (SWITZERLAND) 48:56-62; 1994.*

Synergistic antiproliferative activity of quercetin and cisplatin on ovarian cancer cell growth

It has been demonstrated that the flavonoid quercetin (3,3',4',5-7-pentahydroxyflavone) (Q) inhibits the growth of several cancer cell lines and that the antiproliferative activity of this substance is mediated by a so-called type II estrogen binding site (type II EBS). We investigated the effects of quercetin and cisplatin (CDDP) alone and in combination on the proliferation of the ovarian cancer cell line OVCA 433. Both drugs exhibited a dose-related growth inhibition in a range of concentrations between 0.01 and 2.5 microM and 0.01 and 2.5 micrograms/ml for Q and CDDP

respectively. The combination of the two drugs resulted in a synergistic antiproliferative activity. Two other flavonoids tested, i.e., rutin (3-rhamnosylglucoside of quercetin) and hesperidin [7-b rutinoside of hesperetin (3'-5-3-hydroxy-4-methoxyflavone)] were ineffective both alone and in combination with CDDP. Since both rutin and hesperidin do not bind to type II EBS it can be hypothesized that Q synergizes with CDDP by acting through an interaction with these binding sites.*Scambia G, Ranelletti FO, Benedetti Panici P, et al. Synergistic antiproliferative activity of quercetin and cisplatin on ovarian cancer cell growth. Anticancer Drugs (ENGLAND) , 1:45-48; 1990.*

Inhibitors of biosynthesis of leukotrienes in the treatment of acute pancreatitis

The results of the use of inhibitors of biosynthesis of leukotrienes in the treatment of acute pancreatitis in the experiment and clinic are discussed. Quercetin in a tablet or gel form was used. Treated were 68 patients, of them, 29 were operated on. A high effectiveness of the method in preventing aggravation of destruction of the pancreatic gland is shown.*Zemskov VS, Kolesnikov EB, Luik AI, et al. Inhibitors of biosynthesis of leukotrienes in the treatment of acute pancreatitis. Klin Khir (USSR) 31-33; 1987.*

Antiproliferative activity of quercetin on normal bone marrow and leukaemic progenitors

We used an in vitro clonogenic assay in semi-solid medium to test the sensitivity of normal bone marrow and acute myeloid and lymphoid leukaemia progenitors to the flavonol quercetin. We have studied 14 acute myeloid (AML) and four acute lymphoid (ALL) leukaemias. All ALL and the vast majority of AML (12/14) had a high sensitivity to quercetin with more than 50% growth inhibition at 2 x 10(-6) M quercetin. One M3-AML was partially quercetin-sensitive displaying 60% surviving AML-colony forming units (CFU-AML) at a quercetin concentration of 10(-5) M. One M1-AML was resistant to the growth inhibitory effect of quercetin at a concentration of 2 x 10(-5) M. The clonogenic efficiency of both AML and ALL positively correlated with leukaemic colony-forming unit (CFU-L) sensitivity to quercetin suggesting that this parameter can be useful in predicting quercetin responsiveness of leukaemic cells. We have also studied the effect of various quercetin concentrations on colony formation by normal bone marrow cells. At a quercetin concentration of 10(-5) M, we observed (in five different experiments) a mean recovery of 53% and 65% of erythroid blast-forming units (BFU-E) and granulocyte-macrophage colony-forming units (CFU-GM), respectively. Thus, normal bone marrow appeared partially resistant to quercetin, being inhibited less than 50% by quercetin concentration higher than 2 x 10(-5). When normal bone marrow were deprived in CD34+ haematopoietic progenitors the resultant population became highly sensitive to quercetin, with a mean recovery of BFU-E and CFU-GM of 5% and 12% of controls respectively in the presence of 2 x 10(-5) M quercetin. Furthermore, CD34 progenitors, positively selected, appeared fully resistant to quercetin concentrations as high as 2 x 10(-5) M. Thus, CD34+ progenitors are a quercetin-resistant component in normal bone marrow. In conclusion, our results further provide a biological basis for the therapeutic use of quercetin, considering that this compound could inhibit leukaemic cell growth without suppressing normal haematopoiesis.*Larocca LM, Teofili L, Leone G, et al. Antiproliferative activity of quercetin on normal bone marrow and leukaemic progenitors. Br J Haematol 79:562-566; 1991.*

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